



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/759,746	01/16/2004	Ester Fernandez-Salas	17355CIP4 (BOT)	6885
51957 7590 03/29/2007 ALLERGAN, INC. 2525 DUPONT DRIVE, T2-7H IRVINE, CA 92612-1599			EXAMINER WANG, CHANG YU	
			ART UNIT	PAPER NUMBER
			1649	
SHORTENED STATUTORY PERIOD OF RESPONSE		MAIL DATE	DELIVERY MODE	
3 MONTHS		03/29/2007	PAPER	

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.		Applicant(s)	
	10/759,746		FERNANDEZ-SALAS ET AL.	
	Examiner		Art Unit	
	Chang-Yu Wang		1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 December 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,3-20,22,45-47,56 and 57 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 3-20, 22, 45-47, 56, 57 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--------------------------------------------------------------------------------------|-------------------------------------------------------------------|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION
Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on December 21, 2006 has been entered.

Status of Application Election/Restrictions

2. Claims 2, 21, 23-44, and 48-55 are canceled. Claims 1, 3-20, 22, 45-47, 56-57 are pending and under examination in this office action.
3. Any objection or rejection of record, which is not expressly repeated in this action has been overcome by Applicant's response.
4. Applicant's arguments filed on December 21, 2006 have been fully considered but they are not deemed to be persuasive for the reasons set forth below.

Specification

5. The objection to specification is maintained because the recitation of 10/757077 as incorporated by reference in the amended first paragraph was not found in the original specification. The amendment filed 7/24/06 is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35

Art Unit: 1649

U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material, which is not supported by the original disclosure, is as follows: the recitation of 10/757077 as incorporated by reference in the amended first paragraph.

Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Rejections/Objections Withdrawn

6. The rejection of claims 45-47 under 35 U.S.C. 112, first paragraph because the specification does not enable the invention commensurate in scope with the claims is withdrawn in response to Applicant's amendment to the claims.

The rejection of claims 1, 3-20, 22, 45-47, 56 and 57 under the judicially created doctrine of obviousness-type double patenting for being unpatentable over claim 60 of copending Application No. 10/732703 ('703) in view of Herreros et al. (Mol. Biol. Cell. 2001. 12: 2947-2960) is withdrawn in response to Applicant's arguments.

Claim Rejections/Objections Maintained

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which

Art Unit: 1649

said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. The rejection of claims 1, 3-20, 22, 45-47, 56 and 57 under 35 U.S.C. 103(a) as being unpatentable over US Patent No. 6762280 (Schmidt et al. issued on Jul 13, 2004, effective filing date Sep 25, 2000) in view of Fernandez-Salas et al. (Society for Neuroscience Abstract Viewer and Itinerary Planner, 2003. Vol 2003, pp. Abstract No. 9.2.) or Fernandez-Salas et al. (Steward et al. Naunyn-Schmiedeberg's Archives of Pharmacology, June 2002. Vol. 365 No. Supplement 2, pp. R19) is maintained for reasons of record in the previous office action.

The request of changing the first authorship of the reference of Steward et al. is acknowledged. The authorship of the reference has been changed.

Applicant argues that the combined references of US Patent No. 6762280 (Schmidt et al.), Fernandez-Salas et al. (Fernandez-Salas I), Fernandez-Salas et al. (Fernandez-Salas II) do not provide suggestion/teaching or motivation that would lead a skilled artisan to make the claimed invention because the combined references do not teach the intended use of the instant invention and change the principle of operation disclosed in Schmidt. Applicant argues that US6762280 (Schmidt et al.) teaches different method with different steps to identify compounds that affect proteolytic activity of BoNT/A from the instant invention because the reference of Schmidt et al. does not teach membrane localization of BoNT/A. Applicant also argues that the reference of Schmidt et al. does not teach a cell-based system to screen for a compound that affects biological persistence of BoNT/A because the biological persistence implies a time period that a BoNT/A is proteolytically active and compounds affecting biological

Art Unit: 1649

persistence might have no affect on proteolytic activity of light chain. Applicant argues that the abstracts of Fernandez-Salas I/II do not provide information of identifying compounds that affect biological persistence of BoNT/A.

10. Applicant's arguments have been fully considered but they are not found persuasive. In response to Applicant's arguments regarding motivation/suggestion, it is noted that

The motivation to combine can arise from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. MPEP. §2144.07.

Specific statements in the references themselves which would spell out the claimed invention are not necessary to show obviousness, since questions of obviousness involve not only what references expressly teach, but what they would collectively suggest to one of ordinary skill in the art. See *CTS Corp. v. Electro Materials Corp. of America* 202 USPQ 22 (DC SNY 1979); and *In re Burckel* 201 USPQ 67 (CCPA 1979).

In considering the disclosure of a reference, it is proper to take into account not only specific teaching of the reference but also the inferences which one skilled in the art would be reasonably be expected to draw therefrom. *In re Preda*, 401 F.2d 825, 159 USPQ 342, 344 (CCPA 1968).

It is not necessary that the claimed invention be expressly suggested in any one or all of the references to justify combining their teachings; rather the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981).

In this case, Schmidt (US Patent No. 6762280) teaches a method for identifying a compound that inhibits/enhances the proteolytic activity of botulinum neurotoxin serotype A (BoNT/A) by incubating neurotoxin with the test compound and a fluorescence labeled substrate, and measuring the fluorescence signal resulting from proteolytic cleavage of the substrate by neurotoxin. Schmidt teaches using an FRET assay of detecting the proteolytic activity of the light chain of BoNT/A

Art Unit: 1649

and an ELISA method to screen a compound that inhibits/enhances the proteolytic activity of the light chain of BoNT/A. Although, Schmidt teaches different methods of identifying proteolytic activity of BoNT/A, the biological persistence of BoNT/A relies on the proteolytic activity of the light chain of BoNT/A to inhibit neurotransmitter release. Accordingly, affecting proteolytic activity of the light chain of BoNT/A would consequently affect the biological persistence of BoNT/A. Thus, the teachings of 'Schmidt provide a motivation and expectation of success in screening for a compound that reduces/increases the biological persistence of BoNT/A by affecting the proteolytic activity of BoNT/A light chain on SNAP25 or other substrates of SNARE proteins since affecting proteolytic activity of the light chain would consequently affect the biological persistence of BoNT/A.

Although Schmidt does not use the cell-based screening system as in the screening steps, the references of Fernandez-Salas et al. I/II provide the steps of the screening method using cell based system because the references teach that the fusion protein of the light chain of BoNT/A to GFP protein is colocalized with SNAP25 after transfected in neurons and the colocalization can be detected by confocal microscopy. The combined teachings of Schmidt et al. and Fernandez-Salas et al. provide a motivation and expectation of success in observing the change of localization of light chain of BoNT/A since cleavage of SNAP25 occurs in an intracellular compartment. It would have been obvious to one of ordinary skill in the art at the time of the instant invention was made to be motivated and have reasonable expectations of success in combining the teachings of Schmidt

Art Unit: 1649

et al. (US Patent No. 6762280) and Fernandez-Salas et al. I/II to screen a compound that affects a biological persistence of a Clostridial toxin by evaluating the localization and enzymatic activity since the biological persistence of BoNT/A relies on the proteolytic activity of the light chain. In addition, the interaction of BoNT/A with its substrate, such as SNAP25, occurs intracellularly and the cleavage of SNAP 25 by the light chain subsequently inhibits exocytosis of synaptic vesicles to affect the biological persistence of BoNT/A. Therefore, one of ordinary skill in the art would have expected success in screening a compound that reduces/increases a biological persistence of a BoNT/A by contacting cells expressing a light chain of BoNT/A with test compounds and evaluating the localization and proteolytic activity of the BoNT/A light chain on SNAP25. Thus, the rejection of claims 1, 3-20, 22 and 45-47 under 35 U.S.C. 103(a) as being unpatentable over US Patent No. 6762280 (Schmidt et al. issued on Jul 13, 2004, effective filing date Sep 25, 2000) in view of Fernandez-Salas et al. (Society for Neuroscience Abstract Viewer and Itinerary Planner, 2003. Vol 2003, pp. Abstract No. 9.2.) or Fernandez-Salas et al. (Naunyn-Schmiedeberg's Archives of Pharmacology, (June 2002) Vol. 365 No. Supplement 2, pp. R19) is maintained.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Art Unit: 1649

11. The rejection of claims 3, 4, 46 and 47 under 35 U.S.C. 112, first paragraph, for failing to comply with the written description requirement and being considered as new matter is maintained for reasons of record in the previous office action.

Applicant argues that the specification supports the limitations of “about 20% to about 300% increase” and “about 10% to about 90% reduction” because the limitations were fully supported by US application No. 10757077 ('077), which is incorporated by reference.

12. Applicant's arguments have been fully considered but they are not persuasive. In response, the recitation of 10/757077 as incorporated by reference in the amended first paragraph was not found in the original specification. The recitation of 10/757077 as incorporated by reference would be considered as new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. Thus, the recitations “about 20% to about 300% increase” and “about 10% to about 90% reduction” are considered as new matter because there were no support in the original specification.

Conclusion

NO CLAIM IS ALLOWED.

Art Unit: 1649

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Papers relating to this application may be submitted to Technology Center 1600, Group 1649 by facsimile transmission. The faxing of such papers must

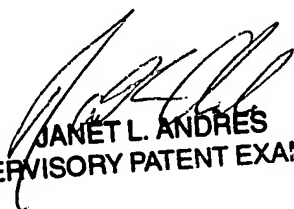
Art Unit: 1649

conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chang-Yu Wang, Ph.D. whose telephone number is (571) 272-4521. The examiner can normally be reached on Monday-Thursday and every other Friday from 8:30 AM to 5:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres, Ph.D., can be reached at (571) 272-0867.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

CYW
March 1, 2007


JANET L. ANDRES
SUPERVISORY PATENT EXAMINER